REMARKS

Claims 37-48 are pending. New Claims 39-48 track prior Claims 19 and 27-35. Independent Claim 39 tracks Claim 19, but further describes "anxiety, depression and memory impairment" as concomitant symptoms and also contains the limitations previously appearing in Claim 25. These concomitant symptoms are disclosed on page 3, first paragraph, of the specification. Accordingly, the Applicants do not believe that any new matter has been added.

The Applicants thank Examiners Lewis and Low for the courteous and helpful interview of March 21, 2006. The Akahane document was reviewed and possible incorporation of new structural or functional limitations into the claims was discussed.

Rejection—35 U.S.C. §102

Claims 19-38 were rejected under 35 U.S.C. 102(b) as being anticipated by Akahane et al., WO 98/03507. The Applicants traverse this rejection since Akahane does not disclose the invention, directed to treatment of Parkinson's disease, with sufficient specificity to amount to an anticipation and only prophetically refers to treatment of Parkinson's disease.

First, Akahane do not exemplify a method of treating Parkinson's Disease and its concomitant symptoms by administering the elected species of compound. Example I on pages 42-43 of Akahane does not describe a method of treatment.

Second, one with ordinary skill in the art would not immediately envisage a method of treating Parkinson's Disease and its concomitant symptoms based on Akahane. While pages 2 and 3 of Akahane prophetically describe a large number of diseases or disorders that might

be treatable using a large genus of pyrazolopyridine compounds, one with skill in the art would not immediately envisage treating Parkinson's Disease and its concomitant symptoms using the elected species of compound based on Akahane.

Review of pages 1-4 shows that Akahane prophetically refers to treatment of a large variety of diverse disorders. However, Akahane does not exemplify or specifically disclose that the subject compound has any effect on Parkinson's disease. Moreover, Akahane is directed to a large genus of compounds of formula (I) (see page 4) and does not envisage selecting a compound for treating Parkinson's Disease, where the compound has an affinity for the adenosine A_1-receptor of the adenosine A_1A_{2a}-receptor dual antagonist that is 0.25 to 40 times greater than its affinity for the adenosine A_{2a}-receptor.

Assuming *arguendo*, that one were to immediately envisage from Akahane treating both Parkinson's Disease and its concomitant symptoms of anxiety, depression and memory impairment (apart from all the different disease states and disorders described by Akahane) by administering a pyrazolopyridine compound, one would not immediately envisage administering a compound having dual A_1 and A_{2a} antagonist activity to subjects having Parkinson's Disease and its concomitant symptoms. For example, the large majority of compounds described by Akahane do not have dual A_1 and A_{2a} antagonist activity. If the large majority of compounds described by Akahane lack dual antagonist activity, one would not immediately envisage treating Parkinson's disease and its concomitant symptoms using a compound having dual antagonist activity as opposed to any of the other compounds disclosed by Akahane.

Moreover, Akahane does not provide an enabling disclosure or any reasonable expectation of success for treating Parkinson's disease. Absent the Applicant's disclosure and experimental data, one with skill in the art would not have been enabled to practice the claimed invention, Since the Akahane treatment of Parkinson's disease is not enabled, this reference cannot anticipate the present invention. "Disclosure of claimed invention in printed publication will not suffice as prior art if it was not enabling", In re Donohue, 226 USPQ 619 (CAFC 1985). Accordingly, the Applicants respectfully request that this rejection be withdrawn.

Rejection—35 U.S.C. §112, first paragraph

Claims 19-37 were rejected under 35 U.S.C. 112, first paragraph, as lacking adequate enablement. These claims are indicated as being enabled for treating catalepsy (in mice), ameliorating impaired memory (in mice), and ameliorating anxiety-like behavior (in Wistar rats) with 3-[2-(thiazole-2-ylmethyl)-3-oxo-2,3-dihydro-pyridizin-6-yl]-2-phenylpyrazolo [1,5-a]pyridine ("the compound of Claim 31").

This rejection is moot for Claims 19-36 which have been cancelled. It does not apply to product Claim 37, because the specification shows how to use compounds having dual A_1A_{2a} receptor antagonist activity for treating disease and exemplifies the activity of this compound in several animal models of catalepsy, impaired memory and anxiety.

It would not apply to new Claims 39-48 because these claims are directed to methods of using compounds having dual A_1A_{2a} receptor antagonist activity, the use of which as noted above is supported by the animal data in the specification. These reasonably support the

activity of the subject compounds with respect to Parkinson's disease. As disclosed on pages 1-2 of the specification, Parkinson's disease patients present with certain mental symptoms such as depression and dementia, but currently available anti-Parkinson's drugs are not effective in controlling these symptoms (page 2, lines 1-8). On the other hand, the specification shows that the subject compounds treat anxiety, depression and memory impairment.

Furthermore, with respect to the scope of enablement issue for the dual A_1A_{2a} receptor antagonist 3-[2-(thiazole-2-ylmethyl)-3-oxo-2,3-dihydro-pyridizin-6-yl]-2-phenylpyrazolo [1,5-a]pyridine ("the compound of Claim 31"), the Applicants have demonstrated that other dual antagonists also exhibit superior pharmacological activity *vis-à-vis* A_1 and A_2 selective antagonists. This is shown in Table 1 (attached at end of this section), which compares the pharmacological activities of A_1 and A_2 selective antagonists with dual A_1A_{2a} receptor antagonists C, D, E, F, G and H (see chemical structures attached at end of this section). As shown in cols. 3-5 of this Table ("Adenosine receptor binding assay") dual antagonists C, D, E, F, G and H meet the limitation in Claim 39 that their affinities for the adenosine A_1-receptor be 0.25 to 40 times greater than their affinities for the adenosine A_{2a}-receptor, see specifically the ratios shown in col. 5.

In view of the nature of the invention which is directed to treating Parkinson's disease and its concomitant symptoms of anxiety, depression and memory impairment using compounds having dual A_1A_{2a} receptor antagonist activity, such as those shown in Table 1 (attached at end of this section), the state of the prior art which only prophetically to treating Parkinson's disease with a genus of compounds which is not selected for dual A_1A_{2a} receptor antagonist activity, the predictability in the art as shown by the experimental data of record, the

high skill of those in the medical and pharmacological arts (e.g., M.D. or Ph.D level), the amount of guidance provided in the specification to select dual agonists as well as animal models of treating anxiety, depression and memory impairment, the actual working examples provided, and the amount of experimentation involved (i.e., selecting a dual agonist and testing its ability to ameliorate Parkinson's disease or its symptoms, such as those shown in the animal models), the Applicant submit that one of skill in the art would be enabled to practice the invention without undue experimentation. Accordingly, the Applicants respectfully request that this rejection be withdrawn.

Table 1. Comparison of efficacies of adenosine antagonists

Adenosine antagonist	Compound	Adenosine receptor binding assay (Ki:nM)			Anticataleptic action (ED50:mg/kg)	Anxiolytic action (Effective dose:mg/kg)		Impaired-memory ameliorating action (Effective dose:mg/kg)	Locomotor activity (Effective dose:mg/kg)
		A_1	A_{2a}	A_{2a}/A_1		Rat social interaction test	Rat elevated plus-maze	Scopolamine-rat passive avoidance test	
A_1 selective	A	6.6	5400	818	>10	3.2	10	0.32, 1.0	No increase
A_{2a} selective	B	>287	9.12	<0.03	0.078	1, 3.2, 10	0.32, 1, 3.2, 10	No effect	0.32, 3.2, 10, 32
Dual	C	0.61	15.5	30.4	0.36	0.32	1, 3.2	0.1, 0.32, 1, 3.2	No increase
	D	0.35	2.46	7.03	0.40	3.2	---	---	3.2, 10
	E	0.11	0.80	7.27	0.11	0.32,1	1, 3.2, 10	0.1, 0.32, 1, 3.2	0.1, 0.32, 1, 3.2
	F	0.36	1.39	3.86	0.06	---	1, 3.2	0.1, 0.32, 1	---
	G	0.43	0.42	0.98	0.075	0.1, 0.32, 1	0.1, 0.32, 1	0.1	0.032, 0.1, 0.32, 1, 3.2, 10
	H	15.16	3.95	0.26	0.276	32	3.2, 10, 32	1, 3.2, 10	---

--- ; not tested,

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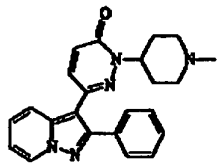
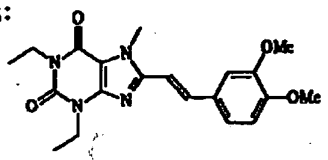
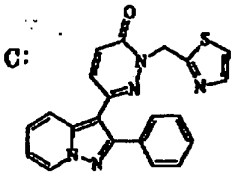
Compound A: 

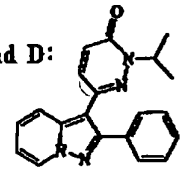
described in WO98/03507.

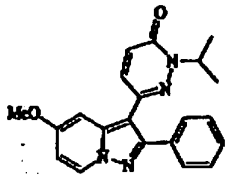
Compound B: 

described in EP0590919.

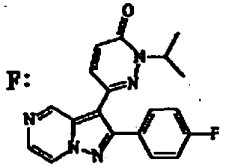
Compound C: 

described in WO98/03507 and this application.

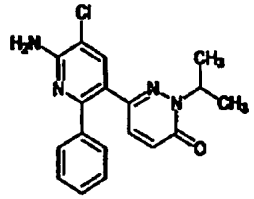
Compound D: 

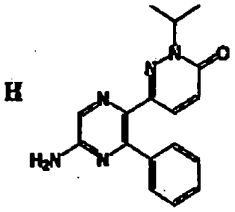
Compound E: 

described in WO02/18382.

Compound F: 

described in WO01/40230.

Compound G 

Compound H 

described in WO2005/095384

CONCLUSION

In view of the above amendments and remarks, the Applicants respectfully submit that this application is now in condition for allowance. Early notification to that effect is earnestly solicited.

Respectfully submitted,

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